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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/775,938	01/31/2001	Margo Haygood	1133.010US1	3910
21186	7590	10/01/2004	EXAMINER	
SCHWEGMAN, LUNDBERG, WOESSNER & KLUTH, P.A.			KERR, KATHLEEN M	
P.O. BOX 2938			ART UNIT	
MINNEAPOLIS, MN 55402			PAPER NUMBER	
			1652	

DATE MAILED: 10/01/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/775,938

Applicant(s)

HAYGOOD ET AL.

Examiner

Kathleen M Kerr

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 26 April 2004.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 66,67,70-74,88 and 90-92 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 66,67,70-74,88 and 90-92 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☒ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|---|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Application Status

1. In response to a previous Office action, a final rejection (mailed on October 21, 2003), Applicants filed an after-final amendment and response received on February 27, 2004. Said amendment was previously not entered (see Advisory action mailed March 23, 2004) but is now entered by virtue of Applicant's RCE filed April 26, 2004. Said amendment amended Claim 66 and added new Claims 90-92. Thus, Claims 66, 67, 70-74, 88 and 90-92 are pending in the instant Office action and will be examined herein.

Priority

2. As previously noted, the instant application is granted the benefit of priority of a continuation of the international application PCT/US00/21326 filed on August 4, 2000. The instant application is also granted the benefit of priority for the U.S. Provisional Application No. 60/147,283 filed on August 4, 1999; the Examiner notes that the elected SEQ ID NO:37 is NOT disclosed in this priority document.

Withdrawn - Claim Rejections - 35 U.S.C. § 112, second paragraph

3. Previous rejection of Claims 66, 67, and 70-74 under 35 U.S.C. § 112, second paragraph, as being indefinite is withdrawn. Applicant has amended the claim to include a defined activity of a domain of a type I polyketide synthase, which functions are clearly defined in the specification and the art as any of KS (ketosynthase), AT (acyltransferase), ACP (acyl carrier protein), DH (dehydratase), ER (enoyl reductase), KR (ketoreductase), and TE (thioesterase).

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4. Previous rejection of Claims 66, 67, and 70-74 under 35 U.S.C. § 112, second paragraph, as being indefinite is withdrawn by virtue of Applicant's amendment defining the complement.

5. Previous rejection of Claims 66, 67, and 70-74 under 35 U.S.C. § 112, second paragraph, as being indefinite for the hybridization conditions in Claim 66 is withdrawn by virtue of Applicant's amendment limiting them as wash conditions (not hybridization conditions).

Withdrawn - Claim Rejections - 35 U.S.C. § 112, first paragraph

6. Previous rejection of Claims 66, 67, and 70-74 under 35 U.S.C. § 112, first paragraph, written description, for having an *unclear function* and being *without any clear structural limitations* is withdrawn by virtue of Applicant's amendment clarifying the structure and function of the claimed subject matter.

NEW or MAINTAINED ISSUES

Objections to the Specification

7. The specification is objected to because on page 16, line 12, the term "thoesterast" is misspelled; the correct spelling is ---thioesterase---. Correction is required.

Claim Rejections - 35 U.S.C. § 112

The following is a quotation of the second paragraph of 35 U.S.C. § 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

8. Claims 66, 67, 70-74, 90, 91, and 92 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject

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matter which applicant regards as the invention. The phrase “wherein the portion includes a domain having at least one activity of a polyketide synthase type I” is unclear as to its metes and bounds. Firstly, activities of modular (type I) PKSs are described on page 16 as including KS, AT, ACP and optionally KR, DH, ER, and TE. Are these the activities intended? Or can other activities be considered such as immunological activities, etc.? The Examiner suggests adding a “wherein” clause to define the PKS activities intended as limiting in the claim.

Additionally, the claims nucleic acid need not be similar to a polyketide synthase I gene provided that it encodes a protein having, for example, dehydratase activity. Since KS, AT, ACP, KR, DH, ER, and TE activities are found in non-PKS enzymes, it must be clear whether or not the claimed invention must be a PKS gene or not. Clarification on these points is required.

9. Claim 67 is rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The limitation of the bryopyran ring is unclear as it depends from Claim 66, wherein the limitation has been removed. Clarification is required.

The following is a quotation of the first paragraph of 35 U.S.C. § 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

10. Claims 70-74 are rejected under 35 U.S.C. § 112, first paragraph, written description, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application

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was filed, had possession of the claimed invention. Claim 70 is drawn to nucleic acid molecules “of Candidatus” thus indicating that the nucleic acid must be native to particular organisms.

To satisfy the written description aspect of 35 U.S.C. § 112, first paragraph, for a claimed genus of molecules, it must be clear that: (1) the identifying characteristics of the claimed molecules have been disclosed, e.g., structure, physical and/or chemical characteristics, functional characteristics when coupled with a known or disclosed correlation between function and structure, or a combination of these; and (2) a representative number of species within the genus must be disclosed.

In the specification, a single example of a proposed PKS gene from Candidatus (or its host organism *Bugula*) that meets the structural limitations of Claim 66 is described – that is, SEQ ID NO:37. No examples of other Candidatus sequences are described within the structural limitations, either PKS sequences or general Candidatus sequences. The instant claims are drawn to a *subgenus* of all PKS genes within the claimed structural limitations, wherein the DNA must be from Candidatus. The specification does not describe Candidatus PKS sequences to the exclusion of PKS sequences from other sources. Clearly, PKS sequences from Candidatus within the structural limitations are enabled by the disclosure; however, one of skill in the art would be unable to recognize other members of the claimed subgenus to the exclusion of, for example, PKS genes from *Streptomyces*, within the structural limitations. Thus, the claimed subgenus does not have adequate written description.

11. Previous rejection of Claims 66, 67, and 70-74 under 35 U.S.C. § 112, first paragraph, scope of enablement, is maintained. Moreover, Claims 90-92 are added to the instant rejection. As previously noted, the instant rejection is set forth as if the utility rejection, maintained below,

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can be overcome in response to the instant Office action. Applicant's arguments have been fully considered but are not deemed persuasive for the following reasons.

Applicant argues that portions of PKS genes would be known how to be used by one of skill in the art; the Examiner does not disagree. Applicant also argues that one of skill in the art could use SEQ ID NO:37 to perform hybridization assays and identify PKS domains having homology so as to make the claimed invention to the full extent of its scope. The Examiner does not disagree with this statement either; however, the claims must be enabled to make, not just to find as Applicant proposes. As previously noted, the specification presents

“no guidance or working examples of the use of polynucleotides that have such low sequence identity with respect to SEQ ID NO:37. The nature of the invention is such that the DNA is purported to encode type I polyketide synthase proteins, and with such a great deviation from the known sequence, the predictability of functionality becomes extremely low. Such enormous breadth and unpredictability renders the instant claims not enabled to the full extent of their scope without undue experimentation. **While the instant specification may describe and enable means for identifying other PKS genes using hybridization methods, etc., these methods do not enable one of skill in the art to make all, or a relevant portion of, the polynucleotides within the scope of the claims because the ability to find a PKS gene, which is structurally related to SEQ ID NO:37, is not equivalent to the ability to make a PKS gene as required by the statute (i.e., “make and use”).** No description in the specification provides particular residues whose encoding is important within the disclosed sequence so that its PKS-nature is maintained. Thus, one of skill in the art would be unable to predict the structure of the other members of the genus in order to make such members. Therefore, the instant claims are not enabled to the full extent of their scope” (emphasis added).

Claim Rejections - 35 U.S.C. § 101

35 U.S.C. § 101 reads as follows:

Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

12. Previous rejection of Claims 66, 67, 70-74 and 88 under 35 U.S.C. § 101 is maintained.

Claims 90-92 are added to the instant rejection. Applicants' arguments have been fully considered but are not deemed persuasive for the following reasons.

Applicant argues by reiterating the isolation procedure for SEQ ID NO:37. To summarize, degenerate primers from an unnamed PKS's KS domain were used to identify KS_a-KS₁ clones (9 clones) in *Bugula*. While Applicant notes that all clones exhibited "significant similarity" (emphasis in original) to other PKS type I genes, no quantitation of said similarity is described. The KS_a clone is then described as aligning to pikAI (a PKS gene) KS domain and to DEBS1; however, this "alignment" is not described in any detail. Moreover, the KS_a clone is NOT SEQ ID NO:37, the claimed invention. The KS_a clone was then used to probe *Bugula* again and contig 5B was isolated; contig 5B is SEQ ID NO:37 and the subject of the claimed invention. Thus, SEQ ID NO:37 is described as having some unnamed homology to the KS_a clone (since it was found via hybridization), and the KS_a clone is reported to have some unnamed homology to pikAI and DEBS1.

Nowhere in the instant specification is the homology of any of the clones reported, more specifically, the homology of SEQ ID NO:37 to any known PKS gene cluster. No open reading frame (encoded protein) is described for SEQ ID NO:37 either in the instant specification or in any post-filing date art the Examiner can find. In the sequence searching of SEQ ID NO:37, no

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homologies to known type I PKSs were found whatsoever. Thus, Applicant's assertion that SEQ ID NO:37 encodes a modular (type I) polyketide synthase is not credible.

The Examiner previously noted that if homologies (alignments) between SEQ ID NO:37 and known PKS type I genes could be provided in prosecution, the asserted utility of SEQ ID NO:37 would be considered. As previously noted,

“the Examiner agrees that if SEQ ID NO:37 could be established as encoding PKSs, by homology, the claimed nucleic acid molecules would have utility; however, Applicant's attention is drawn to the **Guidelines** that **require** the Office to ‘**take into account both the nature and degree of the homology**’. No homology of SEQ ID NO:37 with PKS genes has been established.” (emphasis added)

As previously noted, “[n]o open reading frames and/or encoded proteins are defined for SEQ ID NO:37. No specific function, such as encoding a ketosynthase-functioning enzyme, is proposed for SEQ ID NO:37. No tested functionality of SEQ ID NO:37 is offered, for example, transformation into a bryopyran-minus strain and screening for the introduction of the ability to produce bryopyran compounds.”

Thus, Applicant has offered no arguments that have convinced the Examiner that the assignment of SEQ ID NO:37 encoding a modular PKS is credible. The nature and degree of homology provided by stating (a) the KS_a aligns to pikAI and DEBS1 (without any alignment data) and (b) KS_a hybridizes to SEQ ID NO:37 (without any hybridization conditions) has been considered and is deemed to not give credibility to the utility of the claimed invention.

13. Previous rejection of Claims 66, 67, 70-74 and 88 under 35 U.S.C. § 112, first paragraph, enablement (use), is maintained for the reasons noted above in the maintenance of the utility rejection. Claims 90-92 are added.

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Summary of Pending Issues

14. The following is a summary of the issues pending in the instant application:
- a) The specification stands objected to for the misspelling of "thoesterast".
 - b) Claims 66, 67, 70-74, 90, 91, and 92 stand rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for the nature of the claimed nucleic acid molecule (its activity and/or homology to PKSs).
 - c) Claim 67 stands rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for the limitation of the bryopyran ring.
 - d) Claims 70-74 stand rejected under 35 U.S.C. § 112, first paragraph, written description.
 - e) Claims 66, 67, 70-74 and 90-92 stand rejected under 35 U.S.C. § 112, first paragraph, scope of enablement.
 - f) Claims 66, 67, 70-74, 88, and 90-92 stand rejected under 35 U.S.C. § 101.
 - g) Claims 66, 67, 70-74, 88, and 90-92 stand rejected under 35 U.S.C. § 112, first paragraph, enablement (use).

Conclusion

15. Claims 66, 67, 70-74, 88, and 90-92 are rejected for the reasons identified in the numbered sections of this Office action. Applicants must respond to the objections/rejections in each of the numbered sections in this Office action to be fully responsive in prosecution.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Kathleen M Kerr whose telephone number is (571) 272-0931.

The examiner can normally be reached on Monday through Friday, from 9:00am to 6pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathupura Achutamurthy can be reached on (571) 272-0928. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

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Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).



Kathleen M Kerr
Primary Examiner
Art Unit 1652

September 29, 2004